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Shiftwork in the 21st Century
Challenges for Research and Practice

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The effect of several small time-zone transitions on the timing of salivary melatonin onset.

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Introduction
Flight crew may be required to work outside the hours of the standard 9-to-5 work week and travel across many time-zones. As a result, they often experience difficulty initiating or maintaining sleep, and suffer daytime sleepiness, decreased alertness, impaired performance, and increased fatigue (Klein & Wegmann, 1980; Winget et al, 1984; Wegmann & Klein, 1985). These symptoms, often referred to as ‘jet lag’, typically occur after acute time-zone transitions due to the circadian timing system’s inability to immediately re-train to local external synchronisers, or zeitgebers (ie ‘time givers’).

More than one-hundred human physiological variables have been shown to alter rhythmically with a 24-hour period (Wever, 1979), including body temperature, blood pressure, heart rate, brain neurotransmitter levels, subjective alertness, cognitive performance, and sleepiness (Luce, 1971; Moore-Ede et al, 1982; Lavie, 1986; Dijk et al, 1992). The synchronisation of these variables to a period of 24 hours (ie circadian rhythm) is achieved through entrainment to zeitgebers. For circadian rhythms in humans, the most important zeitgebers are the light/dark cycle and social cues (Klein & Wegmann, 1980; Graeber, 1988).

After single acute time-zone transitions, there is a period of re-entrainment where the desynchronised circadian timing system is ‘reset’ by zeitgebers in the new time-zone. The rate of resynchronisation depends on the number of time-zones crossed and the direction of flight. Typically, the rate of resynchronisation is faster if more time-zones are crossed and flight is in a westward direction (Graeber, 1988), irrespective of the relative direction of flight (ie outgoing or homecoming) or whether flight takes place during the day or night (Klein et al, 1972). More rapid resynchronisation after westward flight occurs because (a) the circadian timing system ‘extends to a period longer than a day (ie about 25 hours) in a free-run environment, facilitating phase delays, and (b) resynchronisation after eastward flight across 8 to 12 time-zones may actually occur through a phase delay (of 12 to 16 hours) rather than a phase advance (Aschoff, 1975; Gundel & Wegmann, 1989).

Most research investigating the physiological effects of transmeridian travel on flight crew has considered the rate of adaptation of the circadian timing system to single acute time-zone transitions (Graeber, 1988). In many operations however, flight crew experience compound time-zone transitions rather than a single shift. The physiological effects of such patterns of time-zone transitions are not well understood. In the current study, the biological adaptation of flight crew to several small time-zone transitions was investigated using salivary melatonin onset as the marker of circadian phase.
Method

Participants
Participants were 14 members of a Royal Australian Air Force (RAAF) Orion P3 aircrew performing a 13-day routine surveillance patrol (SURPAT) throughout the south-west Pacific Ocean. The researcher accompanying the aircrew also completed the experimental protocol, taking the number of participants to fifteen. On average, participants were 30.4 (± 5.1) years of age (mean ± st.dev.), they had worked in the RAAF for 10.1 (± 5.3) years, and had been flying transmeridian missions for 6.4 (± 4.2) years.

Work Schedule
Participants travelled 3.5 time-zones East during the first six days of the SURPAT (the 5th day was a day off), and 3.5 time-zones West during the last seven days of the SURPAT (the 9th and 12th days were days off).

During a typical work day, participants woke before sunrise, commuted to the airport from a local hotel, prepared the aircraft for post-sunrise take-off, flew throughout the day, landed in a new location before sunset, commuted to a local hotel and assembled for debrief, ate dinner and socialised, then went to bed. The average shift duration was 9.3 (± 1.5) hours, of which 6.3 (± 1.3) hours were spent flying.

On days off, participants had complete discretion as to how they spent their time: some slept in, whilst others went sightseeing or did other ‘tourist’ activities. Those who rose from bed earlier on days off typically went to bed earlier the night before, but a few attempted both late nights and early mornings.

Procedure
Sleep
Participants recorded self-determined estimates of sleep onset and wake-up times for major sleep periods and naps for each day of the SURPAT, and for a baseline day prior to the SURPAT. Participants were asked to record this information in sleep diaries as soon as practicable after waking to encourage more accurate recall.

Circadian Phase
The ‘gold standard’ measure of circadian phase is core body temperature (Wever, 1979). However, production of melatonin (a hormone produced by the pineal gland in the suprachiasmatic nucleus) can also be used as a marker of circadian phase as its daily rhythm inversely matches the body temperature cycle (Cagnacci et al, 1992). Melatonin production is extremely low during the daytime, increases markedly during the evening (referred to as ‘melatonin onset’), and is high during the night (Reiter, 1988). In the current study, salivary melatonin onset was used as the marker of circadian phase as the procedure for its measurement is less invasive and has fewer associated stigma than that for core body temperature.

Circadian phase can be determined by monitoring daily timing of melatonin onset: earlier onset indicates a phase advance, whilst later onset indicates a phase delay. The timing of melatonin onset is affected by exposure to light (Czeisler et al, 1989). Generally, as days are shortened (as with eastward flight), the body clock is ‘reset’ and melatonin onset occurs
earlier. Conversely, as days are lengthened (as with westward flight), melatonin onset occurs later.

Participants collected saliva samples on each day of the SURPAT (except for the last day - no samples were collected upon return to home base), and on a baseline day prior to the SURPAT. Single samples were collected in the mid-morning and early afternoon, and hourly samples were collected in the evening (ie from 1800 hrs to sleep onset). There were occasions when some participants were not able to, or forgot to, collect a sample. (For example, pilots and flight engineers missed collecting a sample if this coincided with take-off or landing.) Saliva samples were subsequently analysed for the hormone melatonin by the method of radioimmunoassay (as described by Voultsious et al, 1997).

Data Analysis
The mean (and standard deviation) daytime melatonin level for each participant was determined using their morning and afternoon levels from the baseline day and each day of the SURPAT. For each participant, melatonin onset was defined as the time at which salivary melatonin reached a level at least two standard deviations greater than the mean daytime level (after Voultsious et al, 1997). The group average melatonin onset was then calculated for the baseline day and for each day of the SURPAT (see Figure 1). Biological adaptation was assessed by comparing shifts in the timing of melatonin onset with the magnitude and direction of time-zone transitions.

Results
Figure 1 represents a summary of the sleep, melatonin onset, and time-zone transition data. It is important to note the timing of light exposure over the study period. Between nights 0 and 6, aircrew travelled eastward. Thus, days were effectively shortened as dark occurred relatively earlier. Conversely, aircrew travelled westward between nights 6 and 12, so days were effectively lengthened as dark occurred relatively later.

The length and timing of main sleep periods and the average amount of sleep that participants obtained each day depended on whether or not they worked. On work days, participants woke prior to sunrise and obtained 6.8 (± 1.6) hours of sleep, of which 0.2 hours was napping. On days off, participants slept past sunrise (see nights 4, 8 & 11) and obtained 8.6 (± 2.2) hours of sleep, of which 0.3 hours was napping. Generally, the mean standard error of the mean for sleep onset was greater than for wake-up, indicating a greater variation between participants in the time of sleep onset, than in the time of wake-up. In addition, there was greater variation between participants in the time of wake-up on days off than on work days.

Timing of melatonin onset is reported in Australian Central Standard Time (ACST). Melatonin onset occurred at 2200 hrs on average on the baseline night (+9.5 GMT) and at 1810 hrs on night 6 (-11 GMT). Thus, melatonin onset was advanced 3 hr 50 min following a series of time-zone transitions totalling a 3.5-hr shift to the East during the first six days of the SURPAT. Melatonin onset occurred at 1900 hrs on night 12 (+11 GMT), indicating a phase delay of 50 min following a series of time-zone transitions totalling a 2-hr shift to the West during the second six days of the SURPAT. T-tests indicated that the magnitude of the phase advance between nights 0 and 6 was significant (t=8.2, df=16, p<0.01), whilst the magnitude of the phase delay between nights 6 and 12 was not (t=0.4, df=9, ns).
Figure I. Biological Adaptation to Time-zone Transitions

Legend. Each of the 14 horizontal bars represents a single day of the study (from midday to midday in Australian Central Standard Time). Each bar is labelled on the left and right. The left label refers to the night of the study, from night 0 (the night before the SURFAT began) to night 12; 'BL' is the baseline night. The right label refers to the local time-zone for each night. The white and black areas of the bars represent the timing of light and dark. The smaller white bars represent main sleep periods, with t-bars at either end indicating the variability (standard error of the mean) in sleep onset and awakening times between participants. The white dots represent the time at which melatonin onset occurred on average each evening.
Discussion

If participants had fully adapted to the time-zone transitions throughout the study period, there would have been a phase advance of 3.5 hours between nights 0 and 6 when initially flying eastward, and a phase delay of 2 hours between nights 6 and 12 when subsequently flying westward. However, the phase advance was greater than expected (i.e., 3 hr 50 min), and the subsequent phase delay was less than expected (i.e., 50 min).

Thus, it appears that participants’ ‘body clocks’ adapted well to several small time-zone transitions when initially flying eastward, but did not adapt as well to a similar pattern of time-zone transitions when subsequently flying westward. This finding is contrary to the literature on single acute time-zone transitions which indicates that adaptation to westward flight is more rapid than adaptation to eastward flight (Klein et al., 1972; Graeber, 1988).

However, this counter-intuitive finding may be attributable to factors other than a difference in the ability to adapt to eastward and westward flight after several time-zone transitions.

First, only the timing of melatonin onset was considered, rather than the whole melatonin profile. Thus, it is possible that the shape of the melatonin rhythm may have altered on the eastward and westward periods of the study. For example, a different pattern of results may have emerged if melatonin offset had been considered rather than onset.

Second, the compounding of time-zone transitions and the rapid switch from phase advancing to phase delaying signals (i.e., eastward to westward flight) may have disrupted the circadian timing systems of participants in the second half of the SURPAT. To test this explanation, the current protocol could be repeated with the order of flight direction reversed (i.e., westward first, then eastward). Such a protocol would indicate whether the differential adaptation to westward and eastward flight in the current study was due to the direction of flight itself, or the order in which westward and eastward flight occurred.

Finally, the phase advance during the first half of the SURPAT may not have been solely due to time-zone transitions. The difference in adaptation to eastward and westward flight may be explained by the sleep schedule forced upon participants by the pattern of work during the study period. On the baseline day, participants woke 58 minutes after sunrise. In comparison, on work-days during the eastward period of the SURPAT, participants were required to wake between 52 and 77 minutes prior to sunrise to maximise the time available to fly in daylight. Thus, wake-up occurred 120 to 145 minutes earlier relative to sunrise on these days than on the baseline day. Consequently, there were two phase advancing forces acting on participants’ circadian timing systems during the eastward period of the SURPAT: (1) light ended relatively earlier each evening and began relatively earlier each morning due to the eastward time-zone transitions, and (2) participants were exposed to more light in the morning than in their home time-zone due to their earlier wake-up times. Irrespective of time-zone transitions, increased exposure to light in the morning provides a phase-advancing signal (Czeisler et al., 1989). Thus, the phase advance during the eastward period of the SURPAT may have been due to the earlier wake-up time as well as the time-zone transitions. Ideally, subsequent investigations of the biological adaptation to compound time-zone transitions should control the timing and extent of light exposure in the morning so that the effects of time-zone transitions can be examined independent of the effects of wake-up time.

In summary, salivary melatonin onset was used as a marker of circadian phase to assess the biological adaptation of flight crew to several small time-zone transitions. Results indicated a phase advance greater than expected during the eastward section of the study.
period and a phase delay less than expected during the westward section of the study period. Further research is required to determine whether this counter-intuitive finding occurred because (a) biological adaptation to several small time-zone transitions actually occurs more quickly after eastward than westward flight, (b) the compounding of time-zone transitions and the rapid switch from phase advancing to phase delaying signals disrupted participants’ circadian timing systems, or (c) the sleep schedule forced upon participants by the pattern of work provided a phase advancing signal in addition to the eastward time-zone transitions.

References

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